

What is claimed is:

1. A process for separating a terpene trilactone from Ginkgo biloba plant material or from an extract of Ginkgo biloba comprising a mixture of terpene trilactones, the process comprising the steps of:
  - a) subjecting the Ginkgo biloba plant material or the extract to column chromatography with an appropriate solvent system to produce at least a first fraction containing the terpene trilactone bilobalide, a second fraction eluted after the first fraction containing the terpene trilactones GA and GB, and a third fraction eluted after the second fraction containing at least a preponderance of the terpene trilactones GC and GJ; and
  - b) alkylating the terpene trilactone GB of the second fraction so as to produce a first mixture including terpene trilactone GA and alkylated terpene trilactone GB; or alkylating the terpene trilactone GC of the third fraction so as produce a second mixture including terpene trilactone GJ and alkylated terpene trilactone GC, so as to thereby isolate a terpene trilactone.
2. The process of claim 1, wherein in step a), the solvent system is hexane/ethyl acetate or petroleum ethers/ethyl acetate.

3. The process of claim 1, further comprising triturating the first fraction with a suitable solvent to produce the terpene trilactone bilobalide in at least 95% purity.
4. The process of claim 3, wherein the terpene trilactone bilobalide is produced in at least 98% purity.
5. The process of claim 3, wherein the suitable solvent is ethyl ether.
6. The process of claim 1, wherein the alkylation of the terpene trilactone GB of the second fraction comprises the steps of:
  - a) removing solvent from the second fraction so as to produce a first residue containing at least a preponderance of terpene trilactones GA and GB;
  - b) admixing the first residue in a suitable polar solvent with a suitable base and R-Br,

where R is a substituted or unsubstituted, straight-branched, or cyclic alkyl, or -  
 $\text{CH}_{(2-5)}-\text{Ar}$ ,

where Ar is an aromatic group,

so as to produce a first reaction mixture;
  - c) quenching the first reaction mixture of step b) with a suitable acid;

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  - d) extracting the product of step c) with a first suitable solvent so as to produce a composition comprising terpene trilactone GA and alkylated terpene trilactone GB; and
  - e) triturating the product of step d) with a second suitable solvent, thereby isolating the terpene trilactone GA in at least 95% purity and producing a filtrate containing alkylated terpene trilactone GB.
7. The process of claim 6, wherein in step e) the terpene trilactone GA is isolated in at least 98% purity.
8. The process of claim 6,
- wherein in step a), the solvent is removed under vacuum;
- wherein in step b), the suitable polar solvent is DMF, the suitable base is  $K_2CO_3$  or  $Cs_2CO_3$ , and R-Br is benzyl bromide;
- wherein in step c), the suitable acid is HCl;
- wherein in step d), the first suitable solvent is ethyl acetate; and
- wherein in step e), the second suitable solvent is chloroform.
9. The process of claim 6, further comprising the steps of:

- f) concentrating the filtrate of step e) under vacuum to produce a concentrated filtrate;
  - g) subjecting the concentrated filtrate to column chromatography with a suitable solvent system, thereby separating alkylated terpene trilactone GB from residual terpene trilactone GA; and
  - h) deprotecting the alkylated terpene trilactone GB of step g) by catalytic hydrogenation, thereby obtaining the terpene trilactone GB in at least 95% purity.
10. The process of claim 9, wherein in step h) the terpene trilactone GB is obtained in least 98% purity.
11. The process of claim 9, wherein the suitable solvent system in step g) is hexane/ethyl acetate or petroleum ethers/ethyl acetate.
12. The process of claim 1, wherein the alkylation of the terpene trilactone GC of the third fraction comprises the steps of:
- a) removing solvent from the third fraction so as to produce a second residue containing at least a preponderance of terpene trilactones GJ and GC;
  - b) admixing the second residue in a suitable polar solvent with a suitable base and R-Br,

where R is a substituted or unsubstituted, straight-chained or branched, or cyclic alkyl, or  $-\text{CH}_{(2-5)}-\text{Ar}$ ,

where Ar is an aromatic group,

so as to produce a second reaction mixture;

- c) quenching the second reaction mixture of step b) with a suitable acid;
- d) extracting the product of step c) with a suitable solvent so as to produce a composition comprising terpene trilactone GJ and alkylated terpene trilactone GC;
- e) subjecting the product of step d) to column chromatography with a first suitable solvent system, thereby separating alkylated terpene trilactone GC from terpene trilactone GJ, and providing terpene trilactone GJ in at least 85% purity; and
- f) recrystallizing terpene trilactone GJ from step e) with a second suitable solvent system, thereby providing terpene trilactone GJ in at least 95% purity.

13. The process of claim 12,

wherein in step a), the solvent is removed under vacuum;

wherein in step b), the suitable polar solvent is DMF, the suitable base is  $K_2CO_3$  or  $Cs_2CO_3$ , and R-Br is benzyl bromide;

wherein in step c), the acid is HCl;

wherein in step d), the solvent is ethyl acetate;

wherein in step e), the first suitable solvent system is hexane/ethyl acetate or petroleum ethers/ethyl acetate; and

wherein in step f), the second suitable solvent system is ethanol/water.

14. The process of claim 1, further comprising the step of deprotecting the alkylated terpene trilactone GC of the third fraction by catalytic hydrogenation in a suitable solvent, thereby obtaining the terpene trilactone GC in at least 95% purity.
15. The process of claim 14, wherein the terpene trilactone GC is obtained in at least 98% purity.
16. The process of claim 14, wherein the suitable solvent is ethanol.
17. A composition comprising terpene trilactones GA and GB of step a) of claim 6.
18. A composition comprising terpene trilactone GA and alkylated terpene trilactone GB of step d) of claim 6.

19. A composition comprising terpene trilactones GC and GJ of step a) of claim 12.
20. A composition comprising alkylated terpene trilactone GC and terpene trilactone GJ present of step d) of claim 12.
21. A product prepared by the process of step a) of claim 6.
22. A product prepared by the process of step d) of claim 6.
23. A product prepared by the process of step a) of claim 12.
24. A product prepared by the process of step d) of claim 12.
25. A process for separating a mixture of terpene trilactones GA and GB comprising the steps of:
  - a) dissolving the mixture in a suitable solvent;
  - b) adding benzyl bromide and a suitable base to the mixture, thereby preferentially benzylating terpene trilactone GB;
  - c) separating benzylated terpene trilactone GB from terpene trilactone GA by column chromatography; and
  - d) deprotecting benzylated terpene trilactone GB by catalytic hydrogenation.
26. A process for separating a mixture of terpene trilactones GC and GJ comprising the steps of:
  - a) dissolving the mixture in a suitable solvent;

- b) adding benzyl bromide and a suitable base to the mixture, thereby preferentially benzylating terpene trilactone GC;
- c) separating benzylated terpene trilactone GC from terpene trilactone GJ by column chromatography; and
- d) deprotecting benzylated terpene trilactone GC by catalytic hydrogenation.

27. A process for separating a terpene trilactone from Ginkgo biloba plant material or an extract of Ginkgo biloba comprising a mixture of terpene trilactones, the process comprising the steps of:

- a) subjecting the Ginkgo biloba plant material or the extract to column chromatography with hexane/ethyl acetate to produce at least a first fraction containing the terpene trilactone bilobalide, a second fraction eluted after the first fraction containing the terpene trilactone GA and GB, and a third fraction eluted after the second fraction containing at least a preponderance of the terpene trilactones GC and GJ;
- b) rinsing the first fraction of step a) with ethyl ether to produce the terpene trilactone bilobalide in at least 98% purity;
- c) removing solvent under vacuum from the second fraction in step a) so as to produce a first

residue containing at least a preponderance of terpene trilactones GA and GB; admixing the first residue in DMF with K<sub>2</sub>CO<sub>3</sub> and benzyl bromide, thereby producing a first reaction mixture; quenching the first reaction mixture with HCl, thereby producing a first quenched product; extracting the first quenched product with ethyl acetate, thereby producing a first extracted product; and triturating the first extracted product with chloroform, thereby isolating the terpene trilactone GA in at least 98% purity and producing a filtrate;

- d) concentrating the filtrate of step c) under vacuum to produce a concentrated filtrate; subjecting the concentrated filtrate to column chromatography with hexane/ethyl acetate, thereby separating benzylated terpene trilactone GB from residual terpene trilactone GA; deprotecting the separated terpene trilactone GB by catalytic hydrogenation, thereby obtaining terpene trilactone GB in at least 98% purity;
- e) removing solvent under vacuum from the third fraction of step a) so as to produce a second residue containing at least a preponderance of terpene trilactones GJ and GC; admixing the second residue in DMF with K<sub>2</sub>CO<sub>3</sub> and benzyl bromide, thereby producing a second reaction mixture; quenching the second reaction mixture with HCl, thereby producing a second quenched product; extracting the second quenched product with ethyl acetate, thereby producing a second

extracted product; subjecting the second extracted product to column chromatography with hexane/ethyl acetate, thereby separating benzylated terpene trilactone GC from terpene trilactone GJ, providing terpene trilactone GJ in at least 85% purity; recrystallizing terpene trilactone GJ with ethanol/water, thereby providing terpene trilactone GJ in at least 98% purity; and

- f) deprotecting the benzylated terpene trilactone GC of step e) by catalytic hydrogenation in ethanol, thereby obtaining terpene trilactone GC in at least 95% purity.

28. The process of claim 27, wherein terpene trilactone GJ in step g) is provided in at least 90% purity.
29. The process of claim 27, wherein terpene trilactone GC in step f) is obtained in at least 98% purity.
30. A process for obtaining terpene trilactones from Ginkgo biloba plant material or an extract of Ginkgo biloba comprising a mixture of terpene trilactones, the process comprising the steps of:
- a) extracting the Ginkgo biloba plant material or the Ginkgo biloba extract with a first suitable solvent to produce a first residue and a first filtrate; extracting the first filtrate with a second suitable solvent to produce a second residue and a second filtrate;
  - b) subjecting the second filtrate to column chromatography with a first chromatography system to obtain Bilibalide;

- c) extracting the second residue with a third suitable solvent to obtain terpene trilactone Ginkgolide B (GB) and a third filtrate;
- d) subjecting the third filtrate to column chromatography with a second chromatography system to produce a first fraction containing terpene trilactone Ginkgolide A (GA) and GB and a second fraction containing terpene trilactone Ginkgolide C (GC) and terpene trilactone Ginkgolide J (GJ);
- e) subjecting the first fraction to iterative extractions with a fourth suitable solvent to separate GA and GB; and
- f) subjecting the second fraction to column chromatography with a third chromatography system to separate GC and GJ,  
thereby obtaining terpene trilactones, Bilibalide, GA, GB, GC and GJ isolated from each other and from the Ginkgo biloba plant material or the extract of Ginkgo biloba.

31. The process of claim 30, wherein the first suitable solvent is ethyl acetate.
32. The process of claim 30, wherein the second suitable solvent is diethyl ether.
33. The process of claim 30, wherein the third suitable solvent is methanol.
34. The process of claim 30, wherein the fourth suitable solvent is methanol.

35. The process of claim 30, wherein the first chromatography system comprises hexanes/ethyl acetate.
36. The process of claim 30, wherein the second chromatography system comprises hexanes/acetone.
37. The process of claim 30, wherein the second chromatography system comprises diethyl ether/methanol.
38. The process of claim 30, wherein subjecting the second filtrate to chromatography comprises the steps of:
  - a) concentrating the second filtrate to produce a second concentrated filtrate;
  - b) subjecting the second concentrated filtrate to column chromatography with hexanes/ethyl acetate to produce a fraction containing the terpene trilactone Bilibalide; and
  - c) removing the solvent from the fraction of step b) thereby obtaining the terpene trilactone Bilibalide.
39. The process of claim 30, wherein subjecting the third filtrate to chromatography comprises the steps of:
  - a) concentrating the third filtrate to produce a third concentrated filtrate; and
  - b) subjecting the third concentrated filtrate to column chromatography with hexanes/acetone to produce a first fraction containing a mixture of terpene trilactones Ginkgolide A (GA) and GB and a second fraction containing a mixture of terpene trilactones Ginkgolide C (GC) and Ginkgolide J (GJ).

40. The process of claim 30, wherein extracting the fraction containing a mixture of GA and GB with a fourth suitable solvent to obtain GA and GB comprises the steps of:

- a) removing the solvent from the fraction to produce a residue;
- b) extracting the residue of step a) with methanol to produce a filtrate and GB;
- c) concentrating the filtrate of step b) to produce a concentrated filtrate of step b); admixing the concentrated filtrate of step b) with methanol and filtering to produce a GB enriched residue and a filtrate;
- d) concentrating the filtrate of step c) to produce a concentrated filtrate of step c); admixing the concentrated filtrate of step c) with methanol and filtering to produce a GA enriched residue and a filtrate;
- e) concentrating the filtrate of step d) to produce a concentrated filtrate of step d); admixing the concentrated filtrate of step d) with methanol and crystallizing to produce GA;
- f) admixing the GB enriched residue of step c) and the GA residue of step d) to produce a first residue mixture, which is enriched in GA and GB; admixing the first residue mixture with methanol and filtering to produce GB and a filtrate;
- g) concentrating the filtrate of step f) to produce a concentrated filtrate of step f); admixing the concentrated filtrate of step f) with methanol and filtering to produce GA and a filtrate;
- h) concentrating the filtrate of step g) to produce a concentrated filtrate of step g);

- admixing the concentrated filtrate of step g) with methanol and crystallizing to produce GA,
- i) collecting GA from steps e), g), and h), thereby obtaining GA; and
  - j) collecting the terpene trilacton GB from steps b), and f), thereby obtaining GB.

41. The process of claim 30, wherein subjecting the fraction containing GC and GJ to chromatography comprises the steps of:

- a) concentrating the fraction to produce a concentrated fraction;
- b) subjecting the concentrated fraction to column chromatography with diethyl ether/methanol to produce a GC containing fraction and a GJ containing fraction;
- c) removing the solvent from the GC containing fraction thereby obtaining GC; and
- d) removing the solvent from the GJ containing fraction thereby obtaining GJ.

42. A process for obtaining terpene trilactones from Ginkgo biloba plant material or an extract of Ginkgo biloba comprising a mixture of terpene trilactones, the process comprising the steps of:

- a) extracting the Ginkgo biloba plant material or the Ginkgo biloba extract with ethyl acetate to produce a first residue and a first filtrate;
- b) concentrating the first filtrate of step a) to produce a concentrated first filtrate; extracting the concentrated first filtrate with diethyl ether to produce a second residue and a second filtrate;

- c) concentrating the second filtrate of step b) to produce a second concentrated filtrate; subjecting the second concentrated filtrate to column chromatography with hexanes/ethyl acetate to produce a fraction containing the terpene trilactone Bilibalide;
- d) removing the solvent from the fraction of step c) thereby obtaining the terpene trilactone Bilibalide;
- e) admixing the second residue of step b) with methanol and filtering to produce a third filtrate and the terpene trilactone Ginkgolide B (GB);
- f) concentrating the third filtrate of step e) to produce a third concentrated filtrate; subjecting the third concentrated filtrate to column chromatography with hexanes/acetone to produce a first fraction containing a mixture of terpene trilactones Ginkgolide A (GA) and GB and a second fraction containing a mixture of terpene trilactones Ginkgolide C (GC) and Ginkgolide J (GJ);
- g) removing the solvent from the second fraction of step f) to produce a third residue; subjecting the third residue to column chromatography with diethyl ether/methanol to produce third fraction containing GC and a fourth fraction containing GJ;
- h) removing the solvent from the third fraction of step g) to thereby obtain GC;
- i) removing the solvent from the fourth fraction of step b) to thereby obtain GJ;
- j) removing the solvent from the first fraction of step f) to produce a fourth residue; extracting

- the fourth residue with methanol to produce GB and a fourth filtrate;
- k) concentrating the fourth filtrate of step j) to produce a fourth concentrated filtrate; admixing the fourth concentrated filtrate with methanol and filtering to produce a fifth residue, which residue is GB enriched and a fifth filtrate;
- l) concentrating the fifth filtrate of step k) and to produce a fifth concentrated filtrate; admixing the fifth concentrated filtrate with methanol and filtering to produce an sixth residue, which is GA enriched and a sixth filtrate;
- m) concentrating the sixth filtrate of step l) to produce a sixth concentrated filtrate; admixing the sixth concentrated filtrate with methanol and crystallizing to produce GA;
- n) admixing the fifth residue of step k) and the sixth residue of step l) to produce a first residue mixture, which is enriched in GA and GB; admixing the first residue mixture with methanol and filtering to produce GB and a seventh filtrate;
- o) concentrating the seventh filtrate of step m) to produce a seventh concentrated filtrate; admixing the seventh concentrated filtrate with methanol and filtering to produce an eighth residue, which contains GA and an eighth filtrate;
- p) concentrating the eighth filtrate of step o) to produce a eighth concentrated filtrate; admixing the eighth concentrated filtrate with methonal and crystallizing to produce GA,

q) collecting the GA from steps m), o), and p), thereby obtaining GA; and  
r) collecting the GB from steps e), j), and n), thereby obtaining GB,  
thereby obtaining terpene trilactones.

43. A process for separating each of Bilibalide, Ginkgolide A, (GA), Ginkgolide B, (GB), Ginkgolide C, (GC), and Ginkgolide J, (GJ) from a mixture of terpene trilactones (TTL), wherein the separation is achieved through non-covalent interaction with the mixture of TTLs.

44. A process for isolating bilibalide from a mixture of terpene trilactones (TTL) wherein the mixture comprises Bilibalide, Ginkgolide A, (GA), Ginkgolide B, (GB), Ginkgolide C, (GC), and Ginkgolide J, (GJ), the process comprising the steps of:

- a) extracting the mixture of TTLs with diethyl ether solvent to produce a residue and a filtrate; and
- b) subjecting the filtrate to column chromatography with a hexanes/ethyl acetate solvent system to thereby isolate Bilibalide from the mixture of TTLs.

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new claims 45-63 added, original claims 1-44 unchanged]

45. A process for isolating a ginkgolide from a mixture of terpene trilactones (TTLs) that comprises ginkgolide A, ginkgolide J, ginkgolide C, and ginkgolide B comprising:
  - a) exposing the mixture of TTLs to  $K_2CO_3$  in dimethylformamide;
  - b) adding benzyl-bromide to the product of step a);
  - c) quenching the product of step b) with HCl and extracting with EtOAc and drying with  $MgSO_4$ ; and
  - d) purifying the product of step c) with gradient column chromatography to produce a mixture comprising ginkgolide A and ginkgolide J.
46. The process of claim 45, further comprising purifying the ginkgolide A by recrystallizing from EtOH/H<sub>2</sub>O.
47. The process of claim 45, further comprising purifying the ginkgolide J by recrystallizing from EtOH/H<sub>2</sub>O.
48. A composition comprising ginkgolide J prepared by the method of claim 47.
49. A composition comprising ginkgolide J and ginkgolide A prepared by the method of claim 45.
50. A process for separating a terpene trilactone from Ginkgo biloba plant material or an extract of Ginkgo biloba comprising a mixture of terpene trilactones,

the process comprising the steps of:

- a) subjecting the Ginkgo biloba plant material or the extract to column chromatography with hexane/ethyl acetate to produce at least a first fraction containing the terpene trilactone bilobalide, a second fraction eluted after the first fraction containing the terpene trilactone GA and GB, and a third fraction eluted after the second fraction containing at least a preponderance of the terpene trilactones GC and GJ; and
- b) removing solvent under vacuum from the third fraction of step a) so as to produce a residue containing at least a preponderance of terpene trilactones GJ and GC;
- c) admixing the residue in DMF with K<sub>2</sub>CO<sub>3</sub> and benzyl bromide, thereby producing a reaction mixture;
- d) quenching the reaction mixture with HCl, thereby producing a quenched product;
- e) extracting the quenched product with ethyl acetate, thereby producing a extracted product; and
- f) subjecting the extracted product to column chromatography with hexane/ethyl acetate, thereby separating benzyllated terpene trilactone GC from terpene trilactone GJ, thus providing terpene trilactone GJ in at

least 85% purity.

51. The process of claim 50, wherein the terpene trilactone GJ in step b) is provided in at least 90% purity.
52. The process of claim 50 or 51, further comprising recrystallizing the terpene trilactone GJ with ethanol/water, thereby providing terpene trilactone GJ in at least 98% purity.
53. A process for obtaining a terpene trilactone from Ginkgo biloba plant material or an extract of Ginkgo biloba comprising a mixture of terpene trilactones, the process comprising the steps of:
  - a) extracting the Ginkgo biloba plant material or the Ginkgo biloba extract with a first suitable solvent to produce a first residue and a first filtrate; extracting the first filtrate with a second suitable solvent to produce a second residue and a second filtrate;
  - b) extracting the second residue with a third suitable solvent to obtain terpene trilactone Ginkgolide B (GB) and a third filtrate;
  - c) subjecting the third filtrate to column chromatography with a first chromatography system to produce a first fraction containing terpene trilactone Ginkgolide A

(GA) and GB and a second fraction containing terpene trilactone Ginkgolide C (GC) and terpene trilactone Ginkgolide J (GJ);

- d) subjecting the second fraction to column chromatography with a second chromatography system to separate GC and GJ,

thereby obtaining terpene trilactone GJ isolated from other trilactones and from the Ginkgo biloba plant material or the extract of Ginkgo biloba.

54. The process of claim 53, wherein the first suitable solvent is ethyl acetate.
55. The process of any of claim 53-54, wherein the second suitable solvent is diethyl ether.
56. The process of any of claim 53-55, wherein the third suitable solvent is methanol.
57. The process of any of claim 53-56, wherein the first chromatography system comprises hexanes/acetone.
58. The process of any of claim 53-57, wherein the second chromatography system comprises diethyl ether/methanol.
59. The process of any of claim 53-58, wherein subjecting the third filtrate to chromatography comprises the steps of:

- a) concentrating the third filtrate to produce a third concentrated filtrate; and
- b) subjecting the third concentrated filtrate to column chromatography with hexanes/acetone to produce a first fraction containing a mixture of terpene trilactones Ginkgolide A (GA) and GB and a second fraction containing a mixture of terpene trilactones Ginkgolide C (GC) and Ginkgolide J (GJ).

60. The process of any of claim 53-59, wherein subjecting the fraction containing GC and GJ to chromatography comprises the steps of:

- a) concentrating the fraction to produce a concentrated fraction;
- b) subjecting the concentrated fraction to column chromatography with diethyl ether/methanol to produce a GC containing fraction and a GJ containing fraction;
- c) removing the solvent from the GC containing fraction thereby obtaining GC; and
- d) removing the solvent from the GJ containing fraction thereby obtaining GJ.

61. A process for obtaining a terpene trilactone from ginkgo biloba plant material or an extract of

Ginkgo biloba comprising a mixture of terpene trilactones, the process comprising the steps of:

- a) extracting the Ginkgo biloba plant material or the Ginkgo biloba extract with ethyl acetate to produce a first residue and a first filtrate;
- b) concentrating the first filtrate of step a) to produce a concentrated first filtrate; extracting the concentrated first filtrate with diethyl ether to produce a second residue and a second filtrate;
- c) admixing the second residue of step b) with methanol and filtering to produce a third filtrate and the terpene-trilactone Ginkgolide B (GB);
- d) concentrating the third filtrate of step c) to produce a third concentrated filtrate; subjecting the third concentrated filtrate to column chromatography with hexanes/acetone to produce a first fraction containing a mixture of terpene trilactones Ginkgolide A (GA) and GB and a second fraction containing a mixture of terpene trilactones Ginkgolide C (GC) and Ginkgolide J (GJ);
- e) removing the solvent from the second fraction of step d) to produce a third

residue; and subjecting the third residue to column chromatography with diethyl ether/methanol to produce third fraction containing GC and a fourth fraction containing GJ;

f) removing the solvent from the fourth fraction of step e) to thereby obtain GJ.

62. A process for separating Ginkgolide J (GJ) from a mixture of terpene trilactones (TTLs), wherein the separation is achieved through non-covalent interaction with the mixture of TTLs.

63. A composition comprising ginkgolide J obtained by the process of any one of claims 50 to 62.